REMARKS

Claims 1, 13, 15, 17-20, and 22-24 have been canceled herein without prejudice or disclaimer. Applicant reserves the right to pursue claims encompassing all canceled subject matter in one or more divisional or continuation applications. Claim 11 has been amended to recite the specific amino acid sequences "amino acids 1-46 of SEQ ID NO: 2," "amino acids 47-72 of SEQ ID NO: 2," "amino acids 73-82 of SEQ ID NO: 2," "amino acids 83-106 of SEQ ID NO: 2," "amino acids 112-142 of SEQ ID NO: 2," "amino acids 163-189 of SEQ ID NO: 2," "amino acids 190-213 of SEQ ID NO:2," "amino acids 335-363 of SEQ ID NO:2," "amino acids 364-402 of SEQ ID NO:2," and "amino acids 364-372 of SEQ ID NO:6." Support for the amendment to claim 11 may be found in the specification as originally filed, for example, at page 47, line 1 through page 50, line 5; and page 50, line 19 through page 56, line 21. Currently amended claim11 and previously presented claims 26-47 are pending upon entry of the present amendment in the instant application. No new matter has been added.

Specification

1. The Examiner has requested that Applicant provide a copy of pp.38 for entry into the file to ensure that a legible copy is present when the instant application passes to issue. *See*, Office Action, page 2. Applicant encloses a legible copy of page 38 of the specification as originally filed as requested by the Examiner.

2. The Examiner has objected to the disclosure because of typographical errors at page 262, line 21. *See*, Office Action, page 3. Applicant has amended said errors by replacing the recitations of "300ul" and "600ul" with "300µl" and "600µl" respectively. Given the obvious typographical nature of these errors their correction does not constitute the introduction of new matter.

Rejection under 35 U.S.C. § 101

The Examiner has rejected claims 11 and 26-47 as allegedly "the claimed invention is not supported by a specific, substantial, and credible asserted utility or a well-established utility." *See*, Office Action, page 3. More specifically the Examiner alleges that "the claimed polypeptides lack utility as the claimed utility of a "GPCR neuropeptide receptor" while credible, is not specific or substantial." *See*, Office Action, page 4. Applicant respectfully disagrees and traverses this rejection.

Applicant contends that contrary to the Examiner's allegations, the specification does in fact assert a utility for the claimed invention that satisfies the requirements of 35 U.S.C. § 101. Applicant respectfully points out that the instant specification discloses that the molecule of the claimed invention is a novel member of the G-protein coupled receptor family isolated from a cDNA library prepared from human hypothalamus tissue. *See e.g.*, Page 9, lines 29-32. The specification teaches that the hypothalamus is believed to play a central role in the regulation of feeding behavior and in the control of energy balance in mammals. *See e.g.*, Page 2, lines 16-25. Furthermore, the specification teaches that the claimed invention is useful in the prevention and/or treatment of diseases and disorders including obesity, hyperlipidemia, certain cancers, to stimulate neuronal growth, to regulate neurotransmission, to enhance activity levels and utilization of ingested foods. *See e.g.*, Page 5, lines 11-13. Applicant contends that one of skill in the art could be expected to appreciate the central role of the hypothalamus in the regulation of feeding behavior and in the control of energy balance. Therefore, one of skill in the art could appreciate that the claimed invention may be useful in the prevention and/or treatment of diseases and disorders including obesity and hyperlipidemia. Moreover, these teachings of the specification are further supported by the teaching of exemplary methods by which such a disorder may be treated and/or prevented using compositions of the invention. *See e.g.*, Examples 25-29 at Pages 299-306. Accordingly, Applicant asserts that such characterization of the invention is sufficient to constitute a showing of utility as required under 35 U.S.C. § 101.

The Examiner directs Applicant to the teachings of Sakurai et al. (Cell (1998) 92(4):573-85), and based on Sakurai's identification of a polypeptide having 99.8% identity to the polypeptide of the invention as an orexin receptor (OX1R) further alleges that "[t]he specification as filed does not correctly identify the claimed polypeptides and thus is not specific." *See*, Office Action, page 7. Applicant respectfully disagrees.

As described above, the instant claims are directed to a novel neuropeptide receptor, which is a member of the G-protein coupled receptor family and may be useful in the the prevention and/or treatment of diseases and disorders including obesity and hyperlipidemia. The Examiner has admitted that orexin-A and orexin-B are neuropeptides, which bind the GPCR polypeptide of the instant invention and regulate feeding behavior in mammals. While the specification does not attach the same name as Sakurai et al. to the polypeptide of the instant invention, it is incorrect to conclude that

Applicant has misidentified the polypeptide of the invention when the structure, function and activity of said polypeptide has been described so clearly and accurately.

Furthermore, the post filing publication of Sakurai et al. corroborates that, as first disclosed by Applicant, the claimed invention may be useful in the in the prevention and/or treatment of diseases and disorders including obesity and hyperlipidemia. Sakurai et al. demonstrates that OX1R, the polypeptide of the instant invention, is a neuropeptide receptor member of the G-protein coupled receptor family that regulates feeding behavior in the rat.

Sakurai et al states, in the left column of page 582:

> orexins and their receptors may provide a novel molecular basis for the role of the lateral hypothalamic areas in the regulation of feeding behavior ... pharmacological intervention directed at the orexin receptors may prove to be an attractive avenue toward the discovery of novel therapeutics for diseases involving disregulation of energy homeostasis, such as obesity.

This report clearly shows that expression of OX1R is restricted to the brain, and that its activation stimulates significant increases in food consumption in the rat. As described above, Sakurai et al. also believe that this polypeptide has likely clinical usefulness in the prevention and/or treatment of diseases and disorders including obesity. Accordingly, Applicant asserts that this report demonstrates that the invention as claimed has utility as required under 35 U.S.C. § 101.

Applicant respectfully points out that the specificity of this asserted utility is not called into question by any alleged ability of other proteins to be used in a similar manner. A proper inquiry into utility is simply whether one of skill in the art would more likely than not find it specific, substantial and credible that compositions of the invention, which is preferentially expressed in the hypothalamus, would be useful in the prevention and/or treatment of diseases and disorders including obesity. Applicant notes that an equation of the proper legal requirement of "specific utility" with a "unique utility" is improper. This is clearly not the legal standard for satisfaction of the requirements of 35 U.S.C. § 101. As

described in detail above, the polypeptide of the present invention is preferentially expressed in the hypothalamus and regulates feeding behavior in mammals, and therefore may be used specifically to prevent and/or treat diseases and disorders of feeding behavior including obesity. Therefore, Applicant contends that the asserted utility is specific. Indeed, the M.P.E.P. states that

> [a] "specific utility" is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

See, M.P.E.P. § 2107.01(I) at[2100-32]. Therefore, in light of the directions of the M.P.E.P., Applicant contends that the treatment and/or diagnosis of specific disorders, using specific compositions, constitutes a utility that is "specific to the subject matter claimed" and not "applicable to the broad class of the invention." Accordingly, Applicant respectfully suggests that the Examiner's rejection of the instant claims is not soundly based, and request that it be reconsidered and withdrawn.

Applicant further contends that the specific utility of the instant invention in the prevention and/or treatment of diseases and disorders including obesity is also a substantial utility. The use of compositions of the instant invention in the prevention and/or treatment of such disorders would prove substantially useful and beneficial to people suffering from these and other related disorders. Accordingly, the claimed antibodies of the present invention have a substantial utility as required under 35 U.S.C. § 101.

The Examiner has further alleged that:

> [t]he specification does not disclose any data for any activity for the polypeptide of the amino acid sequence of SEQ ID NO:2 ... the specification contains several assertions of utilities, none of which are supported by data or the prior art. Therefore the claimed polypeptides lack utility

See, Office Action, page 4. Applicant respectfully notes that this assertion is contrary to well established law. The Federal Circuit has recently stated with respect to the rejection of claims for lack of utility that:

> "It is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works." Newman v. Quigg, 877 F.2d 1575, 1581, 11 U.S.P.Q.2D (BNA) 1340, 1345 (Fed. Cir. 1989); see also

> Fromson v. Advance Offset Plate, Inc., 720 F.2d 1565, 1570, 219 U.S.P.Q. (BNA) 1137, 1140 (Fed. Cir. 1983) ("It is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests."). Furthermore, statements that a physiological phenomenon was observed are not inherently suspect simply because the underlying basis for the observation cannot be predicted or explained.

In re Cortright, 49 U.S.P.Q.2d 1464, 1466 (Fed. Cir. 1999). Likewise, according to the axiom of patent law, the utilities asserted for the instant invention do not depend on a proven disclosure of its biological activity. Rather, the issue is whether an asserted utility is more likely than not true to one of ordinary skill in the art. As discussed in detail above, the polypeptide of the instant invention is preferentially expressed in the hypothalamus, it regulates feeding behavior in mammals, and it may be useful in the prevention and/or treatment of diseases and disorders including obesity. Applicant respectfully contends that a nexus has indeed been made between the molecule of the instant invention, the hypothalamus, regulation of feeding behavior and disorders such as obesity. Accordingly, Applicant contends that the asserted utility in the prevention and/or treatment of diseases and disorders including obesity is entirely credible to one of ordinary skill in the art.

In light of the above facts, Applicant contends that the utilities asserted in the specification for the invention as presently claimed are specific, substantial and entirely credible to one of skill in the art. Accordingly, Applicant respectfully requests that the rejection of claims 11 and 26-47 under 35 U.S.C. § 101 be reconsidered and withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Enablement

A. The Examiner has rejected claims 11 and 26-47 as allegedly "since the claimed invention is not supported by a credible, specific and substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." *See*, Office Action, pages 8-9. Applicant respectfully disagrees and traverses this rejection.

For the reasons discussed above in response to the rejection under 35 U.S.C. § 101, the claimed invention is supported by a specific, substantial and well-established utility. Therefore, the Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. §101 rejection is proper." M.P.E.P. § 2107 (IV) at 2100-36. Since the claimed invention complies with the utility

requirement of 35 U.S.C. § 101, the rejection of claims 11 and 26-47 under 35 U.S.C. § 112, first paragraph, based on the alleged lack of utility of the claimed invention, should be withdrawn.

In supporting this rejection the Examiner also alleges that

> the claims are drawn very broadly to fragments, domains, mature forms of a secreted protein, variants, alleles, and species homologues of the polypeptide of SEQ ID NO:2 as well as SEQ ID NO:4 and 6.

See, Office Action, page 9. However, Applicant respectfully points out to the Examiner that claim 11 has been amended, and no pending claim recites "any fragments, domains, mature forms of a secreted protein, variants, alleles, and species homologues of he polypeptide of SEQ ID NO:2 as well as SEQ ID NO:4 and 6." Therefore, this basis for the Examiner's rejection has been obviated. Accordingly, Applicant respectfully requests that the rejection of claims 11 and 26-47 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

B. The Examiner has further rejected claims 11 and 32-37, under 35 U.S.C. § 112, first paragraph, as allegedly containing "subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." *See*, Office Action, page 15.

Preliminarily, Applicant notes that presently rejected claim 11 has been amended so as to no longer recite "ATCC Deposit No: 97128." Accordingly, the present rejection will be addressed in so far as it is understood by Applicant to apply to remaining pending claims.

Applicant has transmitted herewith a Statement by Attorney for Applicant Regarding Permanence and Availability of Deposited Plasmids, which states that the claimed cDNA was accepted by an International Depositary Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon grant of a patent on this application.

In light of the statement made by Applicant's Attorney and the above remarks, Applicant respectfully requests that the rejection of pending claims 11 and 32-37, under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Written Description

The Examiner has rejected claims 38-47 as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." *See*, Office Action, page 13. Applicant respectfully disagrees and traverses this rejection.

The Examiner further alleges that "[t]he claims do not require that the polypeptide possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity. Thus, the claims are drawn to a genus of polypeptides that is defined by sequence identity ... distinguishing characteristics of the claimed genus are not described" *See*, Office Action, page 13. The rejection is respectfully traversed.

In an analysis of written description under 35 U.S.C. § 112, first paragraph, the Examiner bears the initial burden of presenting a *prima facie* case of unpatentability. This burden is only discharged if the Examiner can present evidence or reasons why one skilled in the art would not reasonably conclude that Applicants possessed the subject matter as of the priority date of the present application. *In re Wertheim*, 541 F.2d 257, 262, 191 U.S.P.Q.2d 90, 96 (C.C.P.A. 1976); M.P.E.P. § 2163.04. In the instant case, Applicant maintains that the Examiner has not met this burden.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor had possession of the claimed invention based on the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02. Indeed, as the Federal Circuit has noted, "the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d 989, 54 U.S.P.Q. 2d 1227 (Fed. Cir. 2000) (emphasis added).

Claims 38-47 stand rejected because polypeptides encompassed by the present claims are alleged not to be functionally or structurally limited beyond the amino acid sequence.

It is well established that a "gene is a chemical compound, albeit a complex one". *Amgen, Inc. v. Chugai Pharamceutical Co., LTD.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). Thus, the claims of the instant application, directed to particular polypeptides of the disclosed amino acid sequence of SEQ ID NO:2, as encoded by the nucleic acid sequence of SEQ ID NO:1, are essentially chemical claims involving generic chemical formulae.

As stated by Judge Lourie in *University of California v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997), "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass." All of the objectives met by a generic chemical formula are similarly met by the explicit description in the instant specification of a polynucleotide sequence (*i.e.* SEQ ID NO:1) and the amino acid sequence encoded thereby (SEQ ID NO:2) and by the instant claims to polypeptides which are at least 95% identical to amino acid residues 1 to 425 of SEQ ID NO:2 or the amino acid sequence encoded by cDNA contained in ATCC Deposit No. 97128. That is, the instant claims clearly distinguish the boundaries of the claimed genera and identify all of the members of those genera. Accordingly, one skilled in the art would reasonably conclude that Applicant had possession of the polypeptides encompassed by the rejected claims upon reading the present application as filed, and would immediately recognize that the Applicant had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563). Therefore, the specification contains an adequate written description of the claimed polypeptides. Applicant has provided the skilled artisan with a "generic formula" in the form of the amino acid sequence of SEQ ID NO:2, which indicates "with specificity what the generic claims encompass." Armed with this information "one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass."

Furthermore, the specification particularly discloses embodiments of the invention rejected by the Examiner in the present action. Polypeptides having at least 95% identity to SEQ ID NO:2 are disclosed, for example, at Page 21, line 6 through page 23, line 6. Accordingly, one skilled in the art, enlightened by the teachings of the present application, could readily envision all of the various polypeptide sequences that comprise the specified polypeptides.

For example, the skilled artisan could easily substitute any given amino acid for any other given amino acid, or add or delete amino acids, such that nothing more than what is described in the specification would be required to identify every single one of the polypeptides comprising amino acid sequences that are at least 95% identical to the amino acid sequence of SEQ ID NO:2. Thus, it would be readily apparent to the skilled artisan that the Applicant had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563).

For all of the above reasons, Applicant respectfully asserts that the Examiner has failed to meet the required burden in presenting evidence or reasons why those skilled in the art would not recognize the claimed invention from the disclosure. Moreover, the specification conveys with reasonable clarity that Applicant was in possession of the claimed invention. Therefore, Applicant submits that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the Examiner's rejection of the claims under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Rejection under 35 U.S.C. § 102

A. The Examiner has rejected claim 11 under 35 U.S.C. §§ 102(b) and 102(e), as allegedly being anticipated by US 5,935,814 (10 August 1999) Bergsma & Ellis. Specifically, the Examiner alleges that US 5,935,814 meets "the limitations of claim 11 for a fragment, domain, epitope, mature form, variant, allelic variant, and species homologue. *See*, Office Action, page 17. Applicants respectfully traverse the rejection.

Preliminarily, Applicant notes that presently rejected claim 11 has been amended and no longer recites any one of the group "fragment, domain, epitope, mature form, variant, allelic variant, and species homologue," thereby obviating its rejection as anticipated by US 5,935,814.

Accordingly, Applicant respectfully requests that the present rejection of claim 11, under 35 U.S.C. §§ 102(b) and 102(e), be reconsidered and withdrawn.

B. The Examiner has rejected claims 11, 26, 27, 28, 29, 30, 38, 39, 40, and 41 under 35 U.S.C. §§ 102(a) and 102(e), as allegedly being anticipated by US 6,020,157 (1 February 2000) Bergsma & Ellis (IDS). Specifically, the Examiner alleges that US 6,020,157 "teaches sequences ... meeting the limitations of claim 11 for a fragment, domain, epitope, mature form, variant, allelic variant, and species homologue, as well as claims 26, 38 (Col. 4-6)." *See*, Office Action, page 18. The Examiner further alleges that US 6,020,157 teaches methods and compositions that anticipate the subject matter of dependent claims 27-30 and 39-41. Applicants respectfully traverse the rejection.

Preliminarily, Applicant notes that presently rejected claim 11 has been amended and no longer recites any one of the group "fragment, domain, epitope, mature form, variant, allelic variant, and species homologue," thereby obviating its rejection as anticipated by US 6,020,157.

Furthermore, Applicant respectfully points out that the instant application claims and is entitled to the benefit of priority to PCT International Application Serial No. PCT/US95/05616, filed May 5, 1995. Applicant further points out that US 6,020,157 issued from a US application filed on April 30, 1997, and is therefore unavailable as prior art in the instant application under 35 U.S.C. § 102.

Accordingly, Applicant respectfully requests that the present rejection of claims 11, 26, 27, 28, 29, 30, 38, 39, 40, and 41, under 35 U.S.C. §§ 102(a) and 102(e), be reconsidered and withdrawn.

C. The Examiner has rejected claims 11, 26, 27, 28, 29, 30, 31, 38, 39, 40,41, and 42 under 35 U.S.C. § 102(e), as allegedly being anticipated by US 6,664,229 (16 December 2003) Hagan *et al.* Specifically, the Examiner alleges that US 6,664,229 "teaches sequences ... meeting the limitations of claim 11 for a fragment, domain, epitope, mature form, variant, allelic variant, and species homologue, as well as claims 26, 38 (Col. 4, 10, 13-14)." *See*, Office Action, page 18. The Examiner further alleges that US 6,664,229 teaches methods and compositions that anticipate the subject matter of dependent claims 27-31 and 39-41. Applicants respectfully traverse the rejection.

Preliminarily, Applicant notes that presently rejected claim 11 has been amended and no longer recites any one of the group "fragment, domain, epitope, mature form, variant, allelic variant, and species homologue," thereby obviating its rejection as anticipated by US 6,664,229.

Furthermore, Applicant respectfully points out that the instant application claims and is entitled to the benefit of priority to PCT International Application Serial No. PCT/US95/05616, filed May 5, 1995. Applicant further points out that US 6,664,229 issued from a US application having an earliest claimed priority date of December 15, 1997, and is therefore unavailable as prior art in the instant application under 35 U.S.C. § 102.

Accordingly, Applicant respectfully requests that the present rejection of claims 11, 26, 27, 28, 29, 30, 31, 38, 39, 40,41, and 42, under 35 U.S.C. § 102(e), be reconsidered and withdrawn.

Conclusion

Applicant respectfully requests that the above-made amendments and remarks be entered and made of record in the file history of the instant application. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application.

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Dated: February 28, 2005

Kenley K. Hoover (Reg. No. 40,302)
Attorney for Applicants

Human Genome Sciences, Inc.
14200 Shady Grove Road
Rockville, MD 20850
(301) 610-5771 (phone)

Enclosures
KKH/BM/lcc